7- AND 9- CARBAMATE, UREA, THIOUREA, THIOCARBAMATE, AND HETEROARYL-AMINO SUBSTITUTED TETRACYCLINE COMPOUNDS

60/280,367

Related Applications

This application claims priority to U.S. Provisional Application No. 60/XXX,XXX, filed March 29, 2001, entitled "7- and 9- Carbamate, Urea, Thiourea, Thiocarbamate, and Heteroaryl-Amino Substituted Tetracycline Compounds;" U.S. Provisional Application No. 60/193,972, filed March 31, 2000, entitled "Methods for Synthesizing 7- or 9- Substituted Tetracycline Compounds and Reactive Intermediates;" and to U.S. Provisional Application No. 60/193,879, filed March 31, 2000, entitled "9-Substituted Tetracycline Compounds." The entire contents of all of the aforementioned applications are hereby incorporated herein by reference.

Background of the Invention

The development of the tetracycline antibiotics was the direct result of a systematic screening of soil specimens collected from many parts of the world for evidence of microorganisms capable of producing bacteriocidal and/or bacteriostatic compositions. The first of these novel compounds was introduced in 1948 under the name chlortetracycline. Two years later, oxytetracycline became available. The elucidation of the chemical structure of these compounds confirmed their similarity and furnished the analytical basis for the production of a third member of this group in 1952, tetracycline. A new family of tetracycline compounds, without the ring-attached methyl group present in earlier tetracyclines, was prepared in 1957 and became publicly available in 1967.

Recently, research efforts have focused on developing new tetracycline antibiotic compositions effective under varying therapeutic conditions and routes of administration. New tetracycline analogues have also been investigated which may prove to be equal to or more effective than the originally introduced tetracycline compounds. Examples include U.S. Patent Nos. 3,957,980; 3,674,859; 2,980,584; 2,990,331; 3,062,717; 3,557,280; 4,018,889; 4,024,272; 4,126,680; 3,454,697; and 3,165,531. These patents are representative of the range of pharmaceutically active tetracycline and tetracycline analogue compositions.

Historically, soon after their initial development and introduction, the tetracyclines were found to be highly effective pharmacologically against rickettsiae; a number of gram-positive and gram-negative bacteria; and the agents responsible for lymphogranuloma venereum, inclusion conjunctivitis, and psittacosis. Hence, tetracyclines became known as "broad spectrum" antibiotics. With the subsequent establishment of their *in vitro* antimicrobial activity, effectiveness in experimental infections, and pharmacological properties, the tetracyclines as a class rapidly became widely used for therapeutic purposes. However, this widespread use of tetracyclines for both major and minor illnesses and diseases led directly to